Hindered Rotation About the sp^2–sp^3 Hybridized C–C Bond Between Flavanoid Units in Condensed Tannins

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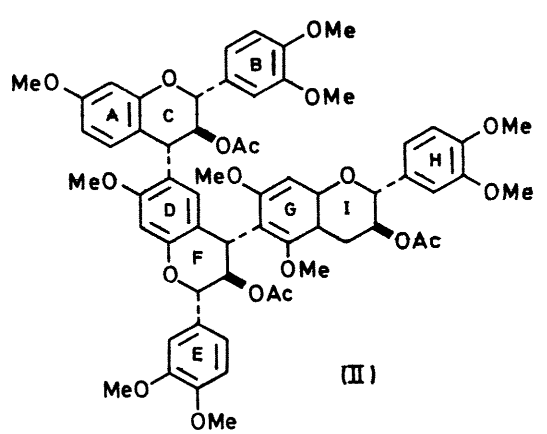
Summary Evidence is provided of rotational isomerism in natural biflavanoid and triflavanoid condensed tannins and of the apparently high incidence of this phenomenon.

THE sp^2–sp^3 hybridized 4,6- or 4,8-links between flavanoid units in bimolecular proanthocyanidins have been recognized as possible points of chirality caused by hindered rotation.[1,2] Although no evidence was available at that time, the likely existence of rotamers was predicted.[1,2] The reported rotational isomerism of synthetic 4-arylpolymethoxyflavans,[3] now prompts us to review our results on the presence and incidence of hindered rotation amongst the natural condensed tannins.

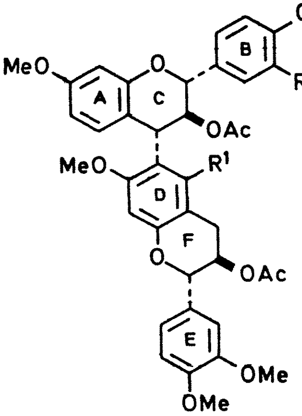
For the recognition of rotational isomerism amongst the methyl ether acetates of di-, tri-, and tetra-meric flavanoids the n.m.r. signals originating from this phenomenon and those from structural isomerism (*i.e.* the alternatives of 4,6- and 4,8-linkages) or impurities must be distinguished.

Rotational isomerism occurs in most polymeric flavonoids from the heartwoods of *Acacia luederitzii*,[4] *A. reficiens*,[4] *A. mearnsii*,[5] *Rhus lancea*, and *Colophospermum mopane*, such random incidence indicating ubiquitous distribution.

Specific examples are dimeric (I) and trimeric (II) profisetinidins from *C. mopane* and dimeric proguibourtinidins (III) from *A. luederitzii*. The n.m.r. spectrum at 220 MHz of the decamethyl ether triacetate of all-*trans* (II) in $CDCl_3$ shows six acetyl signals [τ 8·50 (slight split-double signal), 8·37, 8·32, 8·26, and 8·21] of approximately equivalent intensity instead of the expected three; two split methoxy-signals to high field of the "normal" methoxy-region (pairs at τ 6·99, 7·04 and 6·48, 6·52); two identical pairs of octets at τ 7·12—7·45 and 6·55—6·80, individually typical of 4-methylene signals of the tetramethyl ether of (+)-catechin, and four triplets [τ 3·68, 4·88 (two), 3·99] all of identical



(II)



(I) $R^1 = H, R^2 = OMe$
(III) $R^1 = OMe, R^2 = H$

No decision has yet been possible regarding the alternatives of 4,6- and 4,8-links between the C and D rings of compounds (I) and (II).

coupling constants (ΣJ 20·0 Hz), and typical of 3-protons (c-ring) of 2,3-*trans*-3,4-*trans* upper units of bimolecular flavanoids.[1,2]

At 100 MHz, increase in temperature causes simultaneous and progressive coalescence of the duplicated acetyl and methoxy signals commencing at 41°. The lower field pair of methoxy-(τ 6·48, 6·52) and acetyl (τ 8·26, 8·21) signals resolve into single lines over the range 67—76° while the coalescence of the remaining pairs of methoxy (τ 6·99, 7·04) and acetyl-(τ 8·37, 8·32) signals commences between 58·5 and 67°, and is incomplete at the b.p. (94°) of the $CDCl_3$-hexamethyldisiloxane (*ca.* 15/1 v/v) mixture used as internal lock. This suggests differences in the Arrhenius activation energies for the two interflavanoid bonds.

The same applies to the methyl ether diacetate derivative of all-*trans* biflavanoid (III) from *A. luederitzii* which shows duplication of the 3-H (c-ring) triplet, a split methoxy-signal (τ 6·45, 6·53) and three acetyl signals (τ 8·15, 8·28 and 8·45). These methoxy- and two of the acetyl signals (8·15 and 8·28 integrating as 3H) commence broadening, with reduction in amplitude, from 30° and emerge as single lines at τ 6·39 and 8·22 respectively just below 85°, the b.p. of $CDCl_3$; but the rotations are still incomplete as shown by the different line-width and height of the emergent acetyl (τ 8·22) compared to those of the unaltered acetyl (8·45) signal. During the course of temperature elevation the 3H-triplet is resolved into three single lines.

These data indicate rotational isomerism about both C(sp^2)–C(sp^3) interflavanoid bonds in the trimolecular and the corresponding single bond in the bimolecular tannin and eliminates the alternative of structural isomers or impurities.

Rotomers do not appear to be separable by liquid–liquid countercurrent partition, adsorption and partition chromatography on cellulose (free phenolic form), and subsequent t.l.c. on kieselgel (methyl ethers and methyl ether acetates), although structural isomers based on the alternative 4,6- and 4,8-linkages have been resolved by these methods.[4] From examination of molecular models, methylation of phenolic hydroxy-groups and particularly acetylation of 3-hydroxy-positions must increase the activation energy required for the above thermally induced rotations.

Differences in the activation energy required for rotation about the bonds joining flavanoid units, as shown for the trimeric profisetinidin II, will prove of structural significance.

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